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Acute Suppurative Thyroiditis and Aggressive Malignant Thyroid Tumors: Differences in Clinical Presentation

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Background and Objectives: Aggressive malignant thyroid tumors (AMTT) may mimic the clinical symptoms and signs of acute suppurative thyroiditis (AST) in the early course of the disease process. Our objective was to analyze the clinical features of these two conditions, to assess the best way of early diagnosis, and to propose proper treatment.

Methods: We retrospectively reviewed and analyzed the clinical features of 30 patients, who had similar clinical pictures of AST and were managed at Chang Gung Memorial Medical Center in Linkou, Taiwan, during the period from 1983 to 1996. These patients were consequently diagnosed as either AST or AMTT. The data were analyzed by the Mann-Whitney U, chi-square and Fisher's exact tests.

Results: Among the 30 patients, 25 patients (Male/Female (M/F) ratio = 9/16) were diagnosed as having AST and 5 (M/F ratio = 1/4) as AMTT. After statistical analysis we concluded that the presence of the following factors, namely, older age at diagnosis ($P = 0.0155$), history of dysphonia ($P = 0.0325$), right thyroid lobe involvement ($P = 0.0151$), large size of lesions ($P = 0.0013$), presence of anemia ($P = 0.0075$), and sterile pus cultures from thyroid aspirates ($P = 0.0013$) were cause to suspect a malignancy if the condition did not improve after antibiotics. Delay in diagnosis and management of AMTT may result in a poor prognosis ($P = 0.0082$).

Conclusion: Due to the high mortality rate of AMTT, we should closely observe the patients with poor prognostic variables of acute thyroiditis. Earlier detection and aggressive surgical intervention for AMTT might improve the outcome. *J. Surg. Oncol. 1998;67:28–32.* © 1998 Wiley-Liss, Inc.

KEY WORDS: **acute thyroiditis; sterile pus; prognostic variables**

INTRODUCTION

Acute suppurative thyroiditis (AST) was first described by Bauchet in 1857, and its incidence was about 0.1% of those undergoing thyroid surgery in the preantibiotic era [1]. AST has become exceedingly rare since the advent of antibiotics. AST is most likely diagnosed by the presence of high fever, leukocytosis, and the abrupt onset of an exquisitely tender, tense, erythematous, swelling in the area of the thyroid [2]. The diagnosis of AST depends mostly upon clinical history and findings. Aggressive malignant thyroid tumors (AMTT) were described as having the same clinical features as AST,

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except for the presence of an infectious pathogen in patients with malignant thyroid cancers. The local symptoms and signs of the acute phase of AMTT may mimic those of infectious thyroiditis. Thus, early in the course of AMTT, the differential diagnosis may be difficult. The prognosis of AMTT depends on prompt recognition and appropriate treatment.

Previous reports have rarely discussed the differences between AST and AMTT. In this article we analyze the clinical presentation and laboratory studies of AST and AMTT and attempt to assess the methods of prompt recognition and treatment.

PATIENTS & METHODS

We retrospectively reviewed 30 patients who had similar clinical features as AST, treated at the Chung Gung Memorial Medical Center in Linkou, Taiwan, from 1983 to 1996. An initial finding in all the patients was the presence of numerous polymorphic neutrophils in smears of fine-needle aspirates from thyroid lesions when AST was diagnosed. Most of them had similar clinical symptoms and signs, such as anterior neck pain, tenderness, fever, dysphagia, skin erythema, and dysphonia. All the patients underwent general hematological investigations, such as hemoglobin (Hb), white blood counts (WBC) with differential counts, erythrocyte sedimentation rate (ESR), and pus culture of thyroid aspirates. These patients were initially treated empirically as AST with parenteral antibiotics, such as first- or second-generation cephalosporin and aminoglycoside, then shifted to more effective antibiotics following culture and sensitivity tests. Eleven patients improved promptly after effective antibiotic treatment. Nineteen patients underwent surgical intervention because of recurrent episodes, prolonged course of the acute phase or because of aggravating conditions. They also received thyroid function tests, thyroid ultrasonography and fine-needle aspiration biopsy, thyroid scintigraphy (^{99m}Tc), and radioimage studies such as soft tissue X-rays, computed tomography of the neck, and barium swallows.

The diagnostic criteria of AST were based upon (1) positive thyroid pus cultures, and (2) if sterile, by operative and histological findings or clinical symptoms and signs of acute infection and thyroid lesions that promptly disappear after administration of parenteral antibiotics. AMTT was confirmed by histological examination of thyroid biopsies.

The size of the lesions was determined by real time thyroid ultrasonography, with a 10 MHz transducer (ALOKA, Tokyo, Japan). For suspected thyroid nodules, fine needle aspirations were performed with a 22-gauge needle without local anesthesia. The aspirates were expressed on the center of frosted end glass slides, then stained by the Romanowsky-based Liu-method [3] and Gram stains.

TABLE I. The Clinical Presentations and Laboratory Data of the AST and AMTT Groups**

Parameter	AST	AMTT	*P* value[a]
Age (yrs ± SEM)	35.3 ± 20.9	63.8 ± 21.9	0.0155*
History: dysphonia	7/25 (28%)	4/5 (80%)	0.0325†
Location of lesions			0.0151‡
Right lobe	2/25 (8%)	3/5 (60%)	
Left lobe	17/25 (68%)	1/5 (20%)	
Both lobes	6/25 (24%)	1/5 (20%)	
Size (cm ± SEM)	3.3 ± 1.5	6.0 ± 0.4	0.0013*
Hemoglobin (g/dL ± SEM)	12.4 ± 1.8	9.7 ± 0.8	0.0075*
Pus culture			0.0013†
Positive culture	21/25 (84%)	0/5 (0%)	
Sterile	4/25 (16%)	5/5 (100%)	
Mortality	1/25 (4%)	3/5 (60%)	0.0082†

**SEM, standard error of mean; AST, acute suppurative thyroiditis; AMTT, aggressive malignant thyroid tumor.
[a]Data are calculated by Mann-Whitney U test (*), Fisher's exact test (†), and chi-square test (‡).

We compared and analyzed the variables including gender, age at diagnosis, clinical symptoms and signs, physical findings, preexisting thyroid lesions, general hematological studies (Hb, WBC with differential counts, and ESR), pretreated thyroid function and image studies, pathogens, and mortality rate of the two groups. These results were analyzed by the Mann-Whitney U test for quantitative data, and the coded chi-square test and Fisher's exact test for qualitative data.

RESULTS

The comparison of detailed clinical data of two groups is shown in Table I. Twenty-five of the 30 patients included in this study were diagnosed to have AST and 5 patients had AMTT. The patients in the AST group consisted of nine men and 16 women, and there was one man and four women in the AMTT group. Their mean ages were 35.3 ± 20.9 years (ranging from 1–73 years) and 63.8 ± 21.9 years (ranging from 29–83 years) in the AST and AMTT groups respectively. This difference between the two groups was statistically significant ($P = 0.0155$).

The 30 patients had almost similar clinical features of acute infection over the neck. The symptoms of anterior neck pain, tenderness, fever, dysphagia, dysphonia, erythema, and local heat in the region of the involved thyroid gland, were seen in 100, 100, 96, 56, 20, 96 and 96% respectively of the patients with AST, and in 100, 100, 100, 80, 80, 100, and 100% respectively of those with AMTT. The incidence of dysphonia was the only statistically significant difference between the two groups ($P = 0.0325$). Other symptoms could not be used to differentiate these two groups.

Body temperature, 38.5 ± 1.0°C (ranging from 36.0 to 40.2°C) vs. 38.5 ± 0.7°C (ranging from 37.5 to 39.4°C) respectively for AST and AMTT was not significantly

different ($P = 0.9320$). The consistency of thyroid lesions, 64% hard, 32% elastic, 4% soft in AST group vs. 80% hard, 20% elastic in malignant group, was also not statistically significantly different ($P = 0.7558$). In all patients bruits were absent over the thyroid glands. The locations of thyroid lesions were 68% and 20% located in the left lobe, 8% and 60% in the right lobe for the AST and AMTT groups respectively, with a statistically significant difference at $P = 0.0151$.

The size of the thyroid lesions was determined by thyroid ultrasonography. The mean sizes of two groups were 3.3 ± 1.5 cm (ranging from 1.0 to 8.5 cm) and 6.0 ± 0.4 cm (ranging from 5.0 to 6.5 cm) respectively. This result revealed a smaller area of involvement for the AST group ($P = 0.0013$). Both groups had preexisting thyroid lesions, such as nodular goiter, in 48% and 40% respectively, but no statistically significant difference ($P = 0.87$) was found by the Fisher's exact test. Only one patient presented with hyperthyroidism in the AST group. This 27-year-old man had no preexisting thyroid lesion, and experienced the intermittent high fever and classic symptoms and signs of AST. Mild hyperthyroidism was documented by thyroid function test. Serum T4 level was 13.3 μg/dL (normal ranging from 4.8 to 12.8 μg/dL) by radioimmune assay. He recovered to euthyroid status after the clinical improvement of AST. The other 29 patients were euthyroid. Thyroid functional status could not be used to differentiate between the two groups ($P = 0.363$).

Laboratory studies demonstrated the hemoglobin (12.4 ± 1.8 vs. 9.7 ± 0.8 gm/dL), leukocytosis (68% vs. 100%), and ESR (56.1 ± 26.1 vs. 47.4 ± 17.8 mm/hr) for AST and AMTT groups respectively. Anemia could be used as a predictive factor, with a statistically significant difference at $P = 0.0075$. Only 21 patients (70%) had thyroid scintigraphy studies: 19 cases in the AST group and 2 of the malignant group. Four patients of the AST group had a negative ^{99m}Tc thyroid scan. Cold areas were seen in other patients, but there was no significant difference between the two groups. The pus culture of thyroid aspirates showed 36% gram-positive, 40% gram-negative, 8% anaerobic, and 16% sterile cultures for the AST group. There was no growth in any of the aspirates from the malignant group. This result suggests that we should consider other disorders if a sterile pus culture is found. The pathogens found in the AST group are listed in Table II.

The five patients with AMTT (Table III) were histologically confirmed. Two patients with anaplastic cancers and the one with an unknown primary carcinoma, died within 3 months after histological confirmation. The patient with papillary thyroid carcinoma underwent a total thyroidectomy, ^{131}I ablation therapy and thyroxine suppression therapy. She is alive and well 38 months later and continues to be followed up regularly. The lymphoma patient was managed with chemotherapy, and is alive and well 19 months later.

TABLE II. Summary of Pathogens From Pus Specimens of Acute Suppurative Thyroiditis

Organisms		No. of patients
Gram-positive bacteria	9	
Staphylococcus auerus		2
Staphylococcus epidermidis		1
Streptococcus viridans		1
Group D Streptococcus		2
Other gram-positive bacteria		3
Gram-negative bacteria	10	
Klebsiella pneumoniae		2
Escherichia coli		4
Pseudomonas spp.		1
Acinetobacter		1
Other gram-negative bacteria		2
Anaerobes	2	
Sterile pus	4	
Total	25	

TABLE III. Final Histopathology, Results of Treatment and the Follow-Up Period of Five Patients With Aggressive Malignant Thyroid Tumors*

Pathology type	No. of patients	Death	Follow-up period
Anaplastic cancer	2	2	1–3 mo
Papillary cancer	1	0	38 mo
Metastatic cancer[a]	2	1	1 mo (D), 19 mo (S)
Total	5	3	

*mo, month(s); D, death; S, survival.
[a]Lymphoma (1) and unknown primary carcinoma (1)

One patient in the AST group died of severe systemic septicemia, although strongly effective parenteral antibiotics were prescribed. Three (60%) patients in all, from the AMTT group, died of the disease. The outcome was a statistically significant difference ($P = 0.0082$) for the two groups.

DISCUSSION

AST is a progressive and potentially fatal disease, in which prompt diagnosis and proper treatment usually result in full recovery. Mortality could ensue if these patients were not diagnosed rapidly and accurately, and treated properly. Adequate antibiotics with timely surgical interventions are sufficient to treat AST. In practice, if the clinical symptoms and signs did not improve after one week of antibiotic treatment, surgical drainage and tissue diagnosis became necessary. Patients with thyroid cancer have presented with clinical and biochemical features of AST. Metastatic cancers, anaplastic thyroid cancers, and esophageal carcinoma may masquerade as AST because of tumor necrosis or fistulous tract extending into the perithyroidal area [4,5].

In the early phase, AMTT is difficult to differentiate

from AST. Age usually affects the incidence of malignancy [6,7]. Women are generally affected more often than men in thyroid disorders [7–9]. Our data revealed that male to female ratio were 9/16 and 1/4 respectively. These results were compatible with that of previous reports. However, gender cannot be used as a predictive factor for AMTT.

AST has the classic features of acute infection. Most diagnoses can be made by observing the clinical symptoms [8–11]. However, we found that a rapidly growing malignant tumor with central necrosis could easily cause confusion in making a proper diagnosis. AMTT has symptoms that are similar to AST, such as anterior neck pain, tenderness, fever, dysphagia, erythema, and local heat in the region of the involved thyroid gland. We noted that dysphonia was the only symptom to distinguish between them. Dysphonia could be due to large tumors compressing the recurrent laryngeal nerve or invading the trachea and/or vocal cords.

The left lobe involvement in AST has been reported in previous studies, especially in the presence of a piriform sinus fistula (PSF) [10–12]. The existence of a PSF was not documented in our study. According to our study, right lobe involvement rather than that of the left lobe ($P = 0.0151$) can be regarded as a predictive factor for malignancy. The body temperature, consistency of the thyroid lesions, and bruits on thyroid auscultation did not appear to have any statistically significant difference. An elevated body temperature and hard consistence of thyroid lesions could only hint to the presence of acute inflammation.

The size of lesions has not been discussed with regard to AST. There is evidently a lager major diameter of the lesion in the group with malignancy. This result also explains the possibility of central necrosis within a big mass. Fifty to 67% patients with AST had preexisting thyroid diseases in the previous studies [8,9,13]. Forty-eight percent (12⁄25) of AST had preexisting thyroid lesions in our study. However, we also found that 40% (2⁄5) of patients with AMTT had preexisting thyroid lesions. No statistically significant difference for the presence of preexisting thyroid lesions was calculated.

The normocytic anemia found in the group with AMTT may be due to the effect of increasing erythrocyte consumption of acute inflammation and impairment of erythrocyte production in noninfectious chronic inflammatory disorders of the patients with malignancy [14]. Miyauchi et al. pointed out that leukocytosis and an increased ESR reflected acute inflammation [12]. AMTT had a clinical picture similar to that of acute inflammation in AST. The data on leukocytosis and ESR were compatible with acute inflammatory processes in our study.

Most of the previous studies showed that thyroid function status is euthyroid in AST except for a few case reports that show temporary hyperthyroidism in the acute stage [1,4,11,12]. Only one patient had hyperthyroidism in the AST group of our study. An acute infection might destroy the thyroid follicles and temporarily release the thyroid hormone. A radionuclide scan would show a cold defect in the involved lobe of AST and return to normal after effective therapy [15,16].

The increasing importance of gram-negative organisms was due to changes in the human hosts they infect and to changes in the environment induced by antibiotics and other factors, especially in hospitals [17]. Our results differ from that of previous studies in the prevalence of gram-negative organisms. The prevalence of gram-negative organisms was 7.8% in Berger's study [1]. In our study it was 40% (10⁄25) in the AST group. The difference in prevalence of gram-negative organisms could possibly be due to the differences in race and environment. The finding requires further study. Well-differentiated papillary thyroid carcinoma has also been found to mimic AST because of the necrotic change within the tumor. Thus, a sterile abscess could be a necrotic carcinoma.

The prognosis of AST depends upon correct, early diagnosis, drainage of the lesions and appropriate antibiotics, which have lowered the mortality rate. We believe that papillary thyroid carcinoma and lymphoma would have a better prognosis if they could be rapidly diagnosed and properly managed. We agree with Rosen et al. [18] that where doubt exists as to the diagnosis or response to treatment, open biopsy or surgical intervention may be indicated.

CONCLUSION

AMTT can mimic the clinical features of AST. We propose six risk factors including higher age, the presence of dysphonia, right lobe involvement, lager thyroid mass, presence of anemia, and sterile pus culture, to differentiate AMTT from AST. An aggressive approach might improve the prognosis of AST and of the tumor it mimics.

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